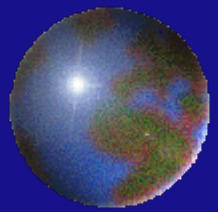

Welcome to Assaying Potency of Novel Vaccines

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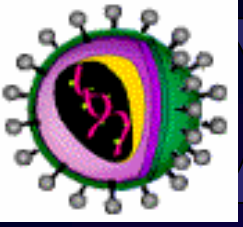
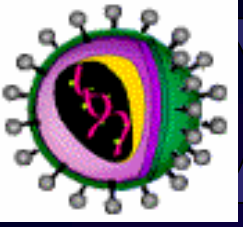
October 11, 2005



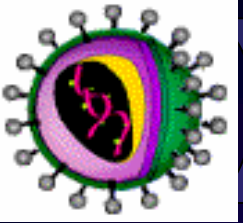
Introduction to Workshop

- HIV/AIDS, Tuberculosis, and Malaria
- Immune Correlates of Protection either not known or incompletely understood
- Validated potency assays need to be implemented for Phase 3 clinical trial lots of vaccines



Background

- Potency would ideally be tied to immune correlates of protection
  - These may/may not be identified after successful Phase 3 trial
- Heterologous prime-boost strategy is a novel challenge
- Vectors are a novel challenge
  - DNA plasmid vaccines
  - Viral vectors or bacterial vectors
  - Replicating, replication-incompetent

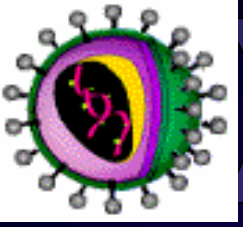


Purpose of Workshop

- To develop consensus on general questions
- To identify research gaps that preclude consensus from being reached

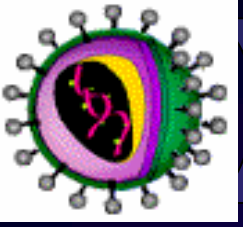
Participants

- Regulators from
  - U.S.
  - South Africa
  - China
  - Thailand
- WHO
- NIH:DMID, VRC, DAIDS
- IAVI
- Industry, grantees, contractors, vaccine developers



APNV questions

- Does vector replication (titer) and in vitro expression correlate sufficiently with immunogenicity to use these two surrogates for vector vaccine potency, or the latter for plasmid vaccine potency?
- How should potency of vaccines that will only be used in combination (i.e., heterologous prime-boost) be measured, since neither vaccine alone can result in protective efficacy? (Releasing a lot of vaccine predicated on another lot of a different vaccine would be problematic)

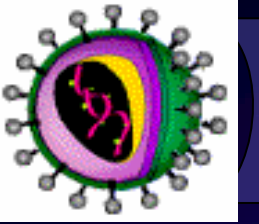


APNV Questions (2)

- For vaccines that are proposed to protect because they induce humoral immunity, what type of assay should be used (neutralization?) and against what targets (e.g., a panel of HIV viruses, the vaccine immunogen)? If neutralization potency must be demonstrated against a panel of viruses/malaria immunogens, how will specifications be set (must similar quantitative values be obtained with each lot for each member of the panel?)
- For vaccines that are proposed to protect because they induce cellular immunity, which assay should be used? Against what targets/antigens (e.g., multiple malaria proteins; multiple clades of HIV; HIV, TB, and malaria antigens for multi-valent products)? How quantitative are these assays ("suitably" as defined by the International Conference on Harmonisation in their Q5C and Q6B documents)?

APNV Questions (3)

- Can in vitro assays rather than bioassays be developed?
- What species should be used for the bioassays? (Does this depend on the assay – i.e., for cellular vs. humoral?)



Format of Workshop

- Introductory session
  - History
  - Regulatory Expectations
- Statistical expectations of potency assays
- Novel assays for novel vaccines
- Round-table discussion
  - All participants to discuss questions, consider consensus

Outcomes

- Slides will be posted on DAIDS website after meeting
- Summary of round-table discussion and consensus or research gaps identified in discussion of questions will also be posted on the DAIDS website
- Funding mechanisms will be considered to address identified research gaps

Let’s get started

- So, welcome to Assaying Potency of Novel Vaccines